JUN - 5 2001

BECKMAN COULTER

510(k) SUMMARY

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

The assigned 510(k) number is: K010429

Submitter's Name and Address

Beckman Coulter, Inc.
1000 Lake Hazeltine Drive
Chaska, MN 55318
Telephone: (952)368-1323
Fax: (952)368-7610
Contact: Brent Taber

Date Prepared: May 24, 2001

Device Names

Proprietary Name: AccuTnI™ and AccuTnI Calibrators on the Access® Immunoassay System
Common Name: Troponin I Enzyme Immunoassay
Classification Name: Immunoassay, Troponin Subunits

Predicate Device

Cardiac Troponin-I (TROP) Method (Dimension® RxL TROP)
Dade Behring Inc.
Newark, DE 19714

510(k) Number: K973650

Device Description

The Access AccuTnI reagents, AccuTnI calibrators and the Access Immunoassay Analyzer comprise the Access Immunoassay System for the quantitative determination of cardiac troponin I in human serum and plasma.

Intended Use

The Access AccuTnI assay is a paramagnetic particle, chemiluminescent immunoassay for the quantitative determination of cardiac troponin I (cTnI) levels in human serum and plasma using the Access Immunoassay Systems to aid in the diagnosis and treatment of myocardial infarction and cardiac muscle damage.

BECKMAN COULTER

Comparison of Technological Characteristics

Parameter	Access AccuTnI	Dimension RxL TROP
Intended Use	For the measurement of cardiac troponin I in human serum and plasma	For the measurement of cardiac troponin I in human serum and plasma
Assay Principles	Utilizes the binding of cardiac troponin I to specific monoclonal antibodies in a two site "sandwich" immunoassay; Utilizes alkaline phosphatase enzyme conjugated to monoclonal antibody	Utilizes the binding of cardiac troponin I to specific monoclonal antibodies in a two site "sandwich" immunoassay; Utilizes alkaline phosphatase enzyme conjugated to monoclonal antibody
Solid Support	Paramagnetic Particles	Chromium Dioxide Particles
Detection System	Utilizes dioxetane-based chemiluminescent substrate; Measures light production from a chemiluminescent reaction	Utilizes flavin adenine dinucleotide phosphate/APO D-amino acid oxidase/horseradish peroxidase as the substrate; Measures color change from an enzyme amplification cascade
Calibrators	Liquid calibrators prepared from buffered bovine serum albumin matrix with recombinant cardiac troponin I complex at specified levels	Liquid calibrators (frozen) prepared from buffered bovine protein matrix and human cardiac troponin I at specified levels
AMI Cutoff	0.50 ng/mL	1.5 ng/mL
Lowest Detectable Level	0.01 ng/mL	0.04 ng/mL

Summary of Analytical Studies

Precision: Within run imprecision ranged from 3.06%CV to 4.42%CV, between-run imprecision ranged from 2.71%CV to 6.07%CV and total imprecision ranged from 4.39%CV to 6.90%CV at levels ranging between 0.42 and 30.55 ng/mL.

Analytical Sensitivity: The lowest detectable level of cTnI distinguishable from zero (Access AccuTnI Calibrator S0) with 95% confidence is 0.01 ng/mL. This value is the mean signal of 10 replicates of the zero calibrator plus two standard deviations. This value is determined by processing a complete six point calibration curve, controls and 10 replicates of the zero calibrator in multiple assays.

Dilution Recovery (Linearity): Linearity studies performed by diluting lithium heparin plasma samples with Access Sample Diluent A provided an average recovery of the samples of 96%, with individual sample average recoveries ranging from 91% to 102%.

Method Comparison: A comparison of cardiac troponin I values from 157 samples, ranging from 0.03 to 44.89 ng/mL (AccuTnI), run with both the Access AccuTnI assay and the Dimension RxL TROP assay demonstrated good agreement with the following statistical data: $y = 0.932x - 1.039$, $r = 0.980$.

BECKMAN COULTER

Matched Sample Comparison: No clinically significant bias was noted between lithium heparin plasma and sodium heparin plasma or serum samples. The AMI cutoff value applies to heparin plasma and serum samples. A study performed by Beckman Coulter, Inc. comparing EDTA plasma samples to heparin plasma samples produced the following correlation: $y = 0.864x - 0.049$, $r = 0.999$.

Analytical Specificity: There was no significant interference from therapeutic drugs, biological substances, heterophile samples or in samples from patients with potentially interfering clinical conditions. There was no significant cross-reactivity with other myofibrillar proteins.

Stability: AccuTnI reagents are stable for 56 days after opening and calibrators are stable for 60 days after opening. The calibration curve is stable for 56 days.

Reference Intervals: The median troponin I value was determined to be 0.01 ng/mL in a healthy population. The 97.5^{th} and 99^{th} percentiles of the reference range were determined to be 0.03 ng/mL and 0.04 ng/mL, respectively.

Equimolarity: The assay recognizes the binary troponin IC or IT or ternary troponin ITC complexes and free cTnI equally. The assay responds to both the phosphorylated and the dephosphorylated forms of cTnI complex equally.

Summary of Clinical Performance

The goals of this multi-site, prospective study were to determine the Beckman Coulter Access AccuTnI cutoff that yields at least 95% sensitivity for diagnosis of AMI and the resulting specificity, and to calculate concordance between the Beckman Coulter Access AccuTnI assay and the Dade Dimension RxL TROP assay.

For this study, 328 patients presenting to a cardiac chest pain center with chest discomfort symptoms lasting more than 20 minutes in the past 24 hours were followed serially to rule-in or rule-out AMI, based on the WHO diagnostic criteria. A minimum of two heparin plasma samples was required from each patient. 74 patients were diagnosed with AMI, and 254 were diagnosed as non-AMI.

AccuTnI values were similar across all sites. Wilcoxon analysis demonstrated that Access AccuTnI values were significantly higher in AMI patients than in non-AMI patients at all sites.

A Levene's test of homogeneity showed no differences in AccuTnI values within the AMI patient group or within the non-AMI patient group across sites.

A Receiver Operating Curve analysis determined that an Access AccuTnI cutoff of 0.50 ng/mL yielded 96% sensitivity, with a corresponding specificity of 94%. It was shown that sensitivity of both the AccuTnI and Dimension RxL assays is highest at 12 to 24 hours after patient admission. Areas Under the ROC curves for both assay formats were compared, (0.98 for AccuTnI and 0.97 for Dimension RxL) and found to be similar, showing both assays are effective in diagnosing AMI.

Concordance between the AccuTnI and the RxL values was calculated. The high 94.6% concordance demonstrated agreement between the two assays in ability to diagnose AMI.

In conclusion, the data provided by this study demonstrate acceptable diagnostic efficiency of the Beckman Coulter Access AccuTnI assay on the Access Immunoassay System, and show equivalent clinical performance to the predicate device.

BECKMAN COULTER

Conclusion

Access AccuTnI and AccuTnI calibrators on the Access Immunoassay System are substantially equivalent to another test currently in commercial distribution for the measurement of cardiac troponin I.

Beckman Coulter, Inc.
1000 Lake Hazeltine Drive
Chaska, MN 55318-1084

Telephone: (612) 448-4848
Internet: www.beckmancoulter.com

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

JUN - 5 2001

Mr. Brent Taber
Regulatory Specialist
Beckman Coulter, Inc.
1000 Lake Hazeltine Drive
Chaska, MN 55318-1084

Re: 510(k) Number: K010429
Trade/Device Name: AccuTnl™ and AccuTnl Calibrators on the Access® Immunoassay System
Regulation Number: 862.1215
Regulatory Class: II
Product Code: MMI, JIS
Dated: April 13, 2001
Received: April 16, 2001

Dear Mr. Taber:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent to devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Good Manufacturing Practice for Medical Devices: General (GMP) regulation (21 CFR Part 820) and that, through periodic GMP inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsma/dsmamain.html".

Sincerely yours,

Steven Gutman

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical Laboratory Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

INDICATIONS FOR USE STATEMENT

510(k) Number (if known): K010429

Device Name: AccuTnI™ and AccuTnI Calibrators on the Access® Immunoassay System

Indications For Use:

The Access AccuTnI assay is a paramagnetic particle, chemiluminescent immunoassay for the quantitative determination of cardiac troponin I (cTnI) levels in human serum and plasma using the Access Immunoassay Systems to aid in the diagnosis and treatment of myocardial infarction and cardiac muscle damage.

Fred Lacy

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K010429

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use ✓
(Per 21 CFR 801.109)

OR

Over-The Counter Use____

(Optional Format 1-2-96)